REMARKS/ARGUMENTS

I. Status of the Claims

Claims 1-16, 18-21, 29-33 are withdrawn

Claims 17, 22-28 are pending

II. U.S. Pat. No. 5,583,046 (Valenta *et al.*,) and Vrtala *et al.*, do not anticipate the pending claims

On page 2 of the Action, the examiner rejected claims 17 and 22-28 under 35 U.S.C. §102 (b) as being anticipated by U.S. Pat. No. 5,583,046, "as evidenced by Vrtala *et al.*" The examiner has not established a legally sufficient basis for a 102 (b) rejection because neither Valenta et al. nor Vrtala et al. either singly or in combination teach all the claimed elements. In addition, there is no justification for adding Vrtala to what should be a rejection based on a single case. Such a combination is an improper and an incorrect basis for an anticipation rejection and even if combined, the combination still does not teach all the elements of the pending claims. The examiner's sole reasoning in support of using Vrtala to fill in the admitted deficiencies in Valenta, is as follows:

> Vrtala recognized that when Betv2 is placed in solution it naturally polymerizes. The Vrtala et al., reference is only relied upon to characterize an already described process.

Action, page 2

To what "solution" in Valenta or in the pending application does the examiner refer? Where is proof of an "already described process?"

A. Valenta does not teach the claimed elements

To anticipate, **a single reference must teach all the elements** of the claims. *RCA Corp v. Applied Digital Data Sys., Inc.*, 221 USPQ 385, 388 (Fed. Cir. 1984). An anticipating prior art reference should disclose **each and every limitation** of the claim expressly or inherently. *Akamai Techs. v. Cable & Wireless Internet Servs.*, 344 F.3d 1186, 1192 (Fed. Cir. 2003). To anticipate a claim, a reference must **disclose every element of the challenged claim and enable** one skilled in the art to make the anticipating subject matter. *PPG Industries, Inc. v. Guardian Industries Corp.*, 75 F.3d 1558, 1566, 37 USPQ2d 1618, 1624 (Fed. Cir. 1996). *(emphases added).*

To stretch beyond one reference, the omitted element must be recognized in the art.

By the examiner's own admission, the '046 (Valenta) patent does not anticipate. The examiner admits that "Claim 17 requires....administering a multimeric profilin" and also admits "The '046 patent.... is silent as to whether Betv2 is multimeric."

As the examiner admits, the '046 patent does not disclose all the claim elements. For example, '046 does not disclose or even suggest the use of a multimeric profilin to hyposensitize a mammal. The '046 patent merely discloses a synthetic version of a 14 kDa birch pollen antigen P14:

> The present invention provides **recombinant DNA molecules** which contain a nucleotide sequence that codes for a polypeptide which exhibits the same or similar antigenic properties as a natural allergen, P14,...(Col. 2, lns. 14-17)
>
> The present invention covers the use of **P14 synthetic polypeptide** allergens to hyposensitize or desensitize a mammal. Such polypeptides can be administered to a human subject either alone or in combination with pharmaceutically acceptable carriers or diluents, in accordance with standard pharmaceutical practice. (Col. 11, lns. 34-40)

In contrast, the claims of the present application are based, in part, on the increased IgE recognition of profilin multimers. Singular fragments based on the sequence that uniquely may arise, or be exposed, upon profilin polymerization that are not available in the monomeric parent molecules. This may reflect one or more novel amino acid sequences that are comprised of part of each of at least two monomers complexed together to form the polymer, or a sequence that is buried within the tertiary monomeric structure that becomes exposed upon multimerization with one or more additional profilins. Such fragments are not dependent upon whether a portion of IgE epitope(s) is present or not. The novel polymers of the present invention takes advantage of native configurations/structural phenomenon that lead to the pan-allergenic potential (not taught in the '046 patent) that, in turn, may be used for diagnostic and therapeutic use to induce a hypoallergenic response.

B. <u>The examiner has not countered applicant's assertion that Vrtala teaches away from the claimed invention</u>

Vrtala **teaches against** the present invention. For example, on page 914, left column, Vrtala states the following:

> It could be shown that rBet v2 formed polymers through disulfide bonds, and it is hence suggested that the **decreased allergenicity of rBet v 2 might be related to its tendency to polymerize**. (emphasis added)

On page 920, left column, Vrtala further states the following:

> [a]nd it is hence possible that the **weaker capacity** of rBet v 2 to induce IgE antibodies might be linked to the ability to form natural **polymers through disulfide bonds**. Although it must be stressed that there is currently no feasible experimental data suggesting that polymerization of antigens might be a mechanism with which to reduce the allergenicity of protein antigens in favor of a TH1 response. (emphasis added)

Therefore, Vrtala teaches away from the present invention which claims profilin multimers with increased allergenicity. The utility of profilin multimers was not recognized in the references cited by the examiner nor are there arguments presented to pinpoint where in solutions of the publication multimeric profilin is formed, and to equate such multimers to those in the present claims.

Vrtala et al. did not find utility for profilin multimers in allergy diagnostics nor therapeutics; they state the opposite.

Their experimental approach does not indicate that profilin multimers would be more allergenic/antigenic and yield possible unique epitopes (upon multimerizing) that could be used as a basis to develop profilin multimer-based diagnostics and immunotherapeutics:

1) The form Vrtala injected into the animal models is not clear, but likely is a monomeric form. Conditions to make a soluble form were followed that would produce mostly monomeric profilin (in Methods: "The recombinant protein produced a single peak in the chromatogram obtained by high-pressure liquid chromatography and was completely soluble").
2) Production of a monomeric form (displayed in Figures 1 and 2) for injection is consistent with the production in animal models of monomeric-recognizing IgG and IgE (lesser degree) shown in Figure 3. Indeed, there were no noted antibodies that recognized the larger profilin forms.
3) 20x of the profilin (Bet v2) was required vs. Bet v1: Vrtala's assumption is because it's due to "some intrinsic property", but "there is currently no feasible experimental model to definitively prove this hypothesis" (page 920, last paragraph).

Considering information in the present application, the reason 20x more of Bet v2 profilin vs. Bet v1 was needed by Vrtala to elicit a response was because the injected solution contained monomers (i.e., weaker allergen/antigen) or undetectably small amounts of

multimers such that a high concentration was needed to achieve an immune response.

III. Summary and Conclusion

Please allow claims as amended. If there are still issues, an interview is requested before proceeding to appeal.

No fees are believed due at this time, however, please charge any additional deficiencies or credit any overpayments to deposit account number 12-0913 with reference to our docket number (21511/92177).

Respectfully submitted,

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